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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,848	07/03/2007	Roberto Pellicciari	0113847.00127US1	3802

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EXAMINER	
BADIO, BARBARA P	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/590,848	PELLICCIARI, ROBERTO	
	Examiner	Art Unit	
	Barbara P. Badio, Ph.D.	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/25/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

First Office Action on the Merits

Claim Rejections - 35 USC § 101

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claims 6-11 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims recite a "use" without setting forth any steps involved in the process and, thus, results in an improper definition of a process, i.e., results in a claim that is not a proper process claim under 35 USC § 101 (see MPEP § 2173.05(q)).

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-12 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 7,138,390. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass 3,7-dihydroxy-6-ethyl-5β-cholanic acid. The difference between the claims is in the position of the 7-hydroxy group. Unlike the cited patent, the instant claims are drawn to the 7β-isomer of the cited compound. However, both chenodeoxycholic acid, i.e., 3α,7α-dihydroxy-5β-cholanic acid and ursdeoxycholic acid, i.e., 3α,7β-dihydroxy-5β-cholanic acid are well known bile acids and, thus, the 7β-isomer of the compound of cited patent is rendered obvious. Additionally, the court has held that a compound that is isomeric with the prior art compound is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compound. In re Norris, 179 F.2d 970, 84 USPQ 458 (CCPA 1970). The present specification lacks showing of any beneficial property possessed by the claimed 7β-isomer not possessed by the 7α-isomer of the cited patent.

5. Claims 1-12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of copending Application No. 11/081,002. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass 6α-ethyl-ursodeoxycholic acid (6EUDCA). Unlike the cited copending Application, the present

claims are limited to 6EUDCA. However, the claimed compound is specially recited by claims 10 and 18 of the cited copending Application and, thus, is anticipated.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Claims 1-12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 24-40 of copending Application No. 11/602,307. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass 3,7-dihydroxy-6-ethyl-5β-cholanic acid. The difference between the claims is in the position of the 7-hydroxy group. Unlike the cited copending Application, the instant claims are drawn to the 7β-isomer of the cited compound. However, both chenodeoxycholic acid, i.e., 3α,7α-dihydroxy-5β-cholanic acid and ursdeoxycholic acid, i.e., 3α,7β-dihydroxy-5β-cholanic acid are well known bile acids and, thus, the 7β-isomer of the compound of cited patent is rendered obvious. Additionally, the court has held that a compound that is isomeric with the prior art compound is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compound. In re Norris, 179 F.2d 970, 84 USPQ 458 (CCPA 1970). The present specification lacks showing of any beneficial property possessed by the claimed 7β-isomer not possessed by the 7α-isomer of the cited patent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 1-12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 11/842,002. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass 3,7-dihydroxy-6-ethyl-5β-cholanic acid. The difference between the claims is in the position of the 7-hydroxy group. Unlike the patent, the instant claims are drawn to the 7β-isomer of the cited compound. However, both chenodeoxycholic acid, i.e., 3α,7α-dihydroxy-5β-cholanic acid and ursdeoxycholic acid, i.e., 3α,7β-dihydroxy-5β-cholanic acid are well known bile acids and, thus, the 7β-isomer of the compound of cited patent is rendered obvious. Additionally, the court has held that a compound that is isomeric with the prior art compound is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compound. In re Norris, 179 F.2d 970, 84 USPQ 458 (CCPA 1970). The present specification lacks showing of any beneficial property possessed by the claimed 7β-isomer not possessed by the 7α-isomer of the cited patent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 1-12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-36, 41 and 43 of copending Application No. 11/914,559. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass

6α-ethyl-ursodeoxycholic acid (6EUDCA). Unlike the cited copending Application, the present claims are limited to 6EUDCA. However, the claimed compound is encompassed by the formula (IC) of claims 1, 41 and 43 and is specifically disclosed on page 17 of the copending Application and, thus, is anticipated.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. It is requested that applicant provide a complete listing of Patents and/or copending Applications which are "material to the patentability" of the present application (see MPEP § 2001.06(b)).

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 6-8 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment, does not reasonably provide enablement for prevention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in In re

Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are (1) the nature of the invention, (2) the breadth of the claims, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the amount of guidance or direction presented, (6) the presence or absence of working examples, (7) the relative skill in the art and (8) the quantity of experimentation necessary. When the above factors are taken into consideration, the examiner's position is that one skilled in the art could not perform the invention commensurate in scope with the instant claim without undue experimentation.

The instant claims contemplate the use of the claimed compounds in the prevention of various disorders. The art teaches a number of treatment regimens for treatment of the various disorders recited by the instant claims. However, there is no known method(s) for the determination of a person susceptible to said disorders and, thus, in need of preventive treatment. The present specification lacks guidance and/or working examples of prevention of any of the claimed disorders. Therefore, in order to practice the claimed invention, the skilled artisan in the art would have to first search the prior art to find, if possible, a model for determination of a person prone to each of the claimed disorder and, thus, in need of preventive treatment. The amount of experimentation necessary to make said determination is undue because of the lack of guidance and/or working examples in the present specification.

12. Claims 6, 7 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are (1) the nature of the invention, (2) the breadth of the claims, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the amount of guidance or direction presented, (6) the presence or absence of working examples, (7) the relative skill in the art and (8) the quantity of experimentation necessary. When the above factors are taken into consideration, the examiner's position is that one skilled in the art could not perform the invention commensurate in scope with the instant claim without undue experimentation.

Claim 6 recites treatment/prevention of "an FXR mediated disease or condition..." and, thus, reads on treatment of any disease, known and unknown, which might be treatable by activation of farnesoid X receptor. Claim 7 recites treatment/prevention of "cardiovascular disease" with no identification of said cardiovascular disease and, thus, read on treatment of known and unknown cardiovascular diseases. Claim 11 recites treatment/prevention of "cholestatic liver disease" with no identification of said disease and, thus, like claims 10 and 18 read on known and unknown diseases.

The present specification lacks correlation between activation of farnesoid X receptors and the treatment/prevention of the scope of diseases encompassed by the instant claims. Thus, the amount of experimentation necessary to practice the claimed invention would not be routine because the skilled artisan in the art would have to first determine the effect of inhibition of farnesoid X receptors in the development of each disease, known and unknown, before determining the effect of activation of said receptors utilizing the claimed compounds on the treatment and/or prevention of said diseases. Said determination would result in undue experimentation.

13. Claims 6, 7 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The present specification discloses the compounds are FXR agonists. However, the present specification fails to provide sufficient descriptive information, such as correlation between activation of farnesoid X receptors and treatment of a representative number of diseases and, thus, lacks adequate description of the presently claimed invention. In other words, the present specification does not convey to the skilled artisan in the art at the time of the present application that applicant had possession of the claimed invention. Adequate written description requires more than a mere indication that the claimed compounds are agonist(s) of farnesoid X receptors.

Some correlation between activation of said receptor and treatment of a representative number of diseases is required.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 3, 6, 7 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite for the following reasons:

(a) Claim 3 lacks a period at the end and (b) Claims 6, 7 and 11 recite the administration of the claimed compound(s) for the treatment and/or prevention of "FXR mediated disease or condition" or "cardiovascular disease" or "cholestatic liver disease". However, they lack recitation of said "FXR mediated disease or condition" or "cardiovascular disease" or "cholestatic liver disease" and, thus, it is unclear what is being treated by administration of the claimed compound(s). The art does not teach treatment/prevention of the scope of diseases encompassed by the instant claims utilizing a single agent and, thus, the skilled artisan would not expect the claimed compounds to be useful in treating all of said diseases.

For these reasons, the metes and bound of the claimed invention is indefinite.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frigerio et al. (EP 312,867).

Frigerio et al. teaches 6-methyl substituted bile acid derivatives such as the 6-methyl derivative of ursodeoxycholic (see the entire article, especially page 3, lines 4-28, 45-53; Example e; claim 2). The reference teaches (a) salts as well as conjugates thereof (see page 3, lines 25-26); (b) the use of the compound(s) in the treatment of biliary calculosis as well as pathological conditions in which a stimulation of biliary flow is required (see page 3, lines 29-32; line 50 – page 4, line 1).

The instant claims differ from the reference by reciting the corresponding 6α-ethyl derivative. However, the prior art compound is the adjacent lower homolog and thus, the claimed invention would have been obvious to one having ordinary skill in the art because the close structural similarity of the reference compound suggests the claimed compound. One skilled in the art would expect the two compounds to have similar properties. In addition, the court has held that adjacent homologs are obvious absent a showing of unexpected and unobvious results. *In re Henze*, 85 USPQ 261, 263. It is

noted that there is no evidence of record of unexpected and obvious properties of the claimed compound(s) versus the prior art compound.

Claims 4 and 5 differ from the reference by reciting a radiolabeled or tritiated compounds. Radiolabeled bile acids and methods of making/using said compounds are known in the art (see for example, US 7,048,907, col. 29, lines 23-53) and, thus, the claimed compounds would be prima facie obvious.

Claims 7-10 further differ from the reference by reciting treatment methods not specifically disclosed by the reference. However, the role of bile acid in the lipid metabolism is well known in the art (see the present specification). Therefore, the claimed methods would have been prima facie obvious to the skilled artisan in the art at the time of the present invention.

Telephone Inquiry

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio, Ph.D. whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Barbara P. Badio, Ph.D./
Primary Examiner, Art Unit 1612